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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,385	09/09/2004	Teizo Yoshimura	4239-64104-02	8908

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EXAMINER	
LEAVITT, MARIA GOMEZ	
ART UNIT	**PAPER NUMBER**
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/507,385	YOSHIMURA, TEIZO	
	Examiner	Art Unit	
	Maria Leavitt	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *1-10 and 23-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09-09-04, 06-27-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response of 02-05-2007 has been entered. With regard to restriction requirements, Applicant's election **with traverse** of Group III (claims 11-22) is acknowledged. Applicant election of the following species is acknowledged: granulocyte-macrophage-colony stimulating factor as the agent that induces the expression of DDR1 (claims 13 and 14), a constitutive promoter as recited on claim 16 and a CD-40 ligand as the additional agent that enhances macrophages or dendritic cell maturation (claim 20).

Response to remarks

Applicant's Arguments of 02-05-2007 in view of the official restriction/ election requirements have been respectfully reconsidered and are found to be persuasive.

On pages 2 and 3 of Applicant's remarks, Applicant argues that the examiner has not carried the burden of providing any reasons and/or examples to support any conclusion that the Groups lack unity of invention. Moreover, Applicant argues that the technical relationship exists among the groups of claims is that activation of DDR1 induces the maturation of an immature macrophage or an immature dendritic cell into a mature macrophage or a mature dendritic cell. Further, applicant contends that macrophages and dendritic cells are not neurons and as such the Bhatt et., reference does not anticipate the claims, their special technical feature and their contribution under prior art. Applicant concludes that the "present application complies with

Rules 13.1 and Rules 13.2 and that the claims should be examined together". Such is not persuasive.

The expression "special technical features" is defined in PCT Rule 13.2 as meaning those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art. The determination is made on the contents of the claims as interpreted in light of the description and drawings (if any). The instant application clearly teaches methods for activation of the discoidin domain receptors (DDRs), and the functional role of said activation in cellular processes such as dendritic cell maturation. The Bhatt et al., reference discloses that activation of the DDRs results in neuronal axon growth, another functional role of said activation. Hence the special technical feature of the instant invention, considered as a whole, does not make a contribution over the prior art. Moreover, a lack of "special technical feature" does not require the use of an "anticipatory" reference as applicant argues. Lack of unity is separate from 35 U.S.C. 102.

The requirement is still deemed proper and is therefore made FINAL.

Therefore, claims 11-22 currently pending for examination to which the following grounds of rejection are applicable.

Specification

On page 28, line 21, the word "sequence" is misspelled. Appropriate correction is required.

Claim Rejections - 35 USC § 102 (a)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 11-16 and 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kamohara et al., (FASEB J. 2001 Dec;15(14):2724-6. Epub 2001 Oct 15),

Kamohara et al., teaches a method of inducing DDR1 expression in both peripheral blood mononuclear cells (PBMC; e.g., lymphocytes and monocytes) and polymorphonuclear neutrophils (PMN) after incubation in RPMI 1640 containing 10% FCS. Moreover, Kamohara et al., discloses that expression level of DDR1 in PBMC was increased further by stimulation with granulocyte-macrophage-colony stimulating factor (GM-CSF) (p. 6, paragraph 4, Results). Human PMN and PBMC were obtained from heparinized blood from human donors and PMN were separated from erythrocytes by lysis (p. 2, paragraph 2). Additionally, Kamohara et al., teaches that the subsequent activation of the DDR1 receptor results in enhanced migration, activation, and differentiation of leukocytes (e.g., neutrophils, lymphocytes, monocytes) during the inflammatory process (p. 2, paragraph 3; p. 10, first paragraph). Kamohara et al., teaches the inducibility of DDR1 expression by binding of collagen to DDR1 transduces intracellular signals necessary for leukocyte functions, including the migration of cells (p. 9, paragraph 4). Kamohara et al., demonstrated up regulation of DDR1 in PMN, monocytes and lymphocytes (p. 10, paragraph 1). Moreover, Kamohara et al., teaches production of mock-infected, DDR1a- or

DDR1b-overexpressing THP-1 cells by transfecting THP-1 with the retroviral vectors pLXSN encoding the full-length human DDR1a- or DDR1b. It is noted that the pLXSN retroviral vector contains promoter/enhancer sequences (see, Clontech pLXSN vector information). Though Kamohara does not teach what cell population is present in PBMC, PBMCs inherently include immature macrophages and dendritic cells. Thus any result of treating the PBMCs with a "DDR activating agent", i.e. transfecting with DDR1b and treating with GM-CSF, would anticipate treatment to any cell in the PBMC population. Current claims 11-18.

Moreover, Kamohara et al., teaches production of mock-infected, DDR1a- or DDR1b-overexpressing THP-1 cells by transfecting THP-1 with the retroviral vectors pLXSN encoding the full-length human DDR1a- or DDR1b. It is noted that the pLXSN retroviral vector contains promoter/enhancer sequences (see, Clontech pLXSN vector information). Current claims 15-16.

Additionally, Kamohara et al., teaches inducibility of DDR1 expression in both PMN and PBMC in vitro (p. 2, last paragraph) and in vivo as shown in Figures 4A and B by numerous mononuclear leukocytes infiltrating the periphery of renal cells carcinomas (p. 7, paragraph 3). Current claims 21 and 22.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 11-19 and 20 rejected under 35 U.S.C. 103(a) as being unpatentable over Kamohara et al., (FASEB J. 2001 Dec;15(14):2724-6. Epub 2001 Oct 15), in view of Lipford et al., (US Pub No. 2003/0148316, Date of Publication August 7, 2003). Kamohara et al., is considered proper prior art as the inventive entity of the Kamohara reference is different from that of the instant application. The only shared inventor between the two is Teizo Yoshimura.

Kamohara et al., teaches a method of inducing DDR1 expression in both peripheral blood mononuclear cells (PBMC; e.g., lymphocytes and monocytes) and polymorphonuclear neutrophils (PMN) after incubation in RPMI 1640 containing 10% FCS. Moreover, Kamohara et al., discloses that expression level of DDR1 in PBMC was increased further by stimulation with granulocyte-macrophage-colony stimulating factor (GM-CSF) (p. 6, paragraph 4, Results). Additionally, Kamohara et al., teaches that the subsequent activation of the DDR1 receptor results in enhanced migration, activation, and differentiation of leukocytes (e.g., neutrophils, lymphocytes, monocytes) during the inflammatory process (p. 2, paragraph 3; p. 10, first paragraph). Kamohara et al., teaches the inducibility of DDR1 expression by binding of collagen to DDR1 transduces intracellular signals necessary for leukocyte functions, including the migration of cells (p. 9, paragraph 4). Further, Kamohara et al., states "functions of inflammatory leukocytes are regulated by up-or down-regulation of cell-surface receptor expression, and subsequent activation and/or deactivation of those receptor by their ligands" (p. 11, paragraph 3).

Kamohara does not specifically teach maturation of dendritic cells in PBMC by another agent such as a CD40 ligand.

However, at the time the invention was made, Lipford et al., teaches the process of maturation of dendritic cells from PBMC by treatment with GM-CSF (p.1, [004] [005]), which is

the same treatment taught in the Kamohara et al., publication to further increase expression of DDR1 and thus enhanced activation and differentiation of the cell populations in PBMC.. Lipford et al., teaches that maturation of dendritic cells to professional APCs can be initiated by T cells expressing CD40 ligand (CD40L)(col. 1, [0004]). In relation to maturation of dendritic cells expressing DDR1 Lipford et al., discloses on page 7, Table 1a, a list of cell surface markers expressed in resting or unstimulated state of myeloid-like DCs precursor DC type 1 (i.e., plasmacytoid dendritic cells, **pDC1**) including DDR1 (Table1a, rank 165, Accession #U48705) and cell surface markers including DDR1 that are induced or upregulated during immunostimulation (p. 18, Table 5c, Rank 17, Accession # U48705; p.2, [0015])). Lipford et al., teaches agents that stimulate pDC including anti-CD40 antibodies (p. 20, [0110]) and discloses the use of such agents in the stimulation and/or attenuation of dendritic cells either *in vivo* or *ex vivo* (p. 27, [0172]). Moreover, Lipford et al., discloses the advantage of using a single marker (and more preferably, a naturally occurring or synthetic ligand to that marker, including an antibody or antibody fragment) in methods directed at stimulating or down regulating pDC activity (p. 2, [0014]).

Therefore, in view of the benefits of inducing DDR1 expression in peripheral blood mononuclear cells (PBMC) in the presence of GM-CSF to induce cell cell migration activation, and differentiation in inflammatory processes as taught Kamohara et al., it would have been *prima facie* obvious to additionally contact immature macrophages or dendritiec cells particularly because Lipford et al., teaches that maturation of dendritic cells to professional APCs can be initiated by T cells expressing CD40 ligand. Further, base on the detailed teachings of the Kamohara publication and the Lipford patent and the high level of skill in the art of

molecular cloning, the skilled artisan would have had a reasonable expectation of success in generating a mature macrophage or dendritic cell by contacting with a GM-CSF, and/or a CD40 ligand, (e.g., antibody) as encompassed by the instant claims.

Conclusion

Claims 11-22 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

To aid in correlating any papers for this application, all further correspondence regarding his application should be directed to Group Art Unit 1636; Central Fax No. (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also

enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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